

Application No.: 09/868581  
Amendment dated: June 14, 2004  
Reply to Office action of February 13, 2004

#### AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application.

#### LISTING OF CLAIMS:

1 (Currently amended). A process for the production of particles of a material wherein:

a stream of a dispersion of the material in a solvent and a stream of a compressible fluid antisolvent substance are brought into contact with each other so that the streams combine to form a mixture under conditions such that the substance is in compressible fluid antisolvent state,

the mixture is then caused to flow along a conduit extending downstream from the region where the streams come into contact, toward an orifice which opens from the conduit directly into a downstream region so that the mixture flows through the orifice into the downstream region,

a back pressure is generated in at least part of the conduit, whereby the pressure and temperature of the mixture in the conduit are such that the compressible fluid antisolvent substance remains in a compressed state over at least part of the length of the conduit, ~~and~~

the conduit is sufficiently long that the residence time of the mixture in the conduit is such that particle formation occurs in the conduit, and

the pressure and temperature in the downstream region are such that the compressible fluid antisolvent

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substance is present therein in a gaseous state and the material separates from the mixture in a particulate state as a consequence of the conversion of the compressible fluid antisolvent into a gas.

2-41 (cancelled)

42 (previously presented). A process according to claim 1, wherein the compressible fluid antisolvent substance is in a supercritical fluid state over at least a part of the length of the conduit.

43 (previously presented). A process according to claim 1, wherein in the downstream region the pressure is in the range from 1-20 bar, and the temperature is in the range from 0-50°C.

44 (currently amended). A process according to claim ~~42~~ 43, wherein, in the downstream region, the pressure is around atmospheric.

45 (previously presented). A process according to claims 1, wherein the compressible fluid antisolvent substance comprises carbon dioxide.

46 (currently amended). A process according to claim ~~44~~ 45, wherein the carbon dioxide is in a supercritical fluid state over at least a part of the length of the conduit.

47 (previously presented). A process according to claim 1, wherein the solvent is an organic solvent selected from C<sub>1-5</sub>

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alkyl C<sub>1-5</sub> alkanoate esters, C<sub>1-5</sub> alcohols, and di- C<sub>1-5</sub> alkyl ketones, halogenated organic solvents, water, and mixtures thereof.

48 (previously presented). A process according to claim 1, wherein the solvent is saturated or near saturated with the material.

49 (currently amended). A process according to claim ~~41~~ 42, wherein the ratio of the flow rate of the stream of said antisolvent substance in a supercritical fluid state to the flow rate of the stream of a dispersion of said material in a solvent is 50:1 or less.

50 (previously presented). A process according to claim 1, wherein one or more solid additives, are introduced, as a dispersion in a carrier vehicle, into the mixture of the material, the solvent and the compressible fluid antisolvent substance.

51 (currently amended). A process according to claim 1, wherein one or more additives, and/or modifiers, are ~~introduced into~~ included in the mixture of the material, the solvent and the compressible fluid antisolvent substance.

52 (currently amended). A process according to claim ~~50~~ 51, wherein the additive and/or modifier is introduced into the stream of dispersion of the material and/or the stream of a compressible fluid antisolvent substance.

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53 (currently amended). A process according to claim ~~50~~ 51, wherein the additive and/or modifier is mixed with one or both of said streams before the streams are brought into contact with each other.

54 (currently amended). A process according to claim ~~50~~ 51, wherein the one or more additives and/or modifiers are separately introduced into the region where the streams are brought into contact with each other.

55 (currently amended). A process according to claim ~~50~~ 51, wherein the one or more additives and/or modifiers are introduced into the mixture of the dispersion and the compressible fluid antisolvent substance at the region where the streams of the dispersion and compressible fluid antisolvent substance are brought into contact with each other.

56 (currently amended). A process according to claim ~~50~~ 51, wherein the one or more additives and/or modifiers are introduced into the mixture of the dispersion and the compressible fluid antisolvent substance, in the conduit between the region where the streams come into contact and the orifice.

57 (currently amended). A process according to claims ~~50~~ 51, wherein the one or more additives is an excipient material.

58 (currently amended). A process ~~according to claim 1,~~ for the production of particles of a material wherein:

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a stream of a dispersion of the material in a solvent and  
a stream of a compressible fluid antisolvent  
substance are brought into contact with each other  
so that the streams combine to form a mixture under  
conditions such that the substance is in  
compressible fluid antisolvent state,

the mixture is then caused to flow along a conduit  
extending downstream from the region where the  
streams come into contact, toward an orifice which  
opens from the conduit directly into a downstream  
region so that the mixture flows through the orifice  
into the downstream region,

the pressure and temperature of the mixture in the  
conduit are such that the compressible fluid  
antisolvent substance remains in a compressed state  
over at least part of the length of the conduit,  
the pressure and temperature in the downstream region are  
such that the compressible fluid antisolvent  
substance is present therein in a gaseous state and  
the material separates from the mixture in a  
particulate state as a consequence of the conversion  
of the compressible fluid antisolvent into a gas,  
and

one or more solid ~~additives~~, additives are introduced, as  
a dispersion in a carrier vehicle, into the mixture  
of the material, the solvent and the compressible  
fluid antisolvent substance, said compressible fluid  
antisolvent substance decompresses from said  
compressed state, and the one or more additives are  
introduced into the mixture of the dispersion and  
the compressible fluid antisolvent substance after

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said compressible fluid antisolvent substance  
decompresses.

59 (cancelled).

60 (currently amended). A process ~~according to claim 58, for~~ forming a co-formulation of a material and an additive in which a mixture of a material and an additive is produced by introducing the additive, in a fluid carrier vehicle, into a mixed stream in a compressed state, the mixed stream comprising the material and a compressible fluid antisolvent substance, and then causing the mixed stream, including the additive, to flow into a downstream region where the compressible fluid antisolvent substance decompresses, and wherein said material and said compressible fluid antisolvent substance are brought together at a location in a conduit, said mixed stream flows toward said downstream region in the conduit, a back pressure is maintained at least in a region of the conduit between said location and said downstream region, and the pressure and temperature of the mixed stream in the conduit are maintained, by said back pressure, at levels such that the compressible fluid antisolvent substance is maintained in a compressible fluid antisolvent state.

61 (currently amended). A process ~~according to claim 58, for~~ forming a co-formulation of a material and an additive in which a mixture of a material and an additive is produced by introducing the additive, in a fluid carrier vehicle, into a mixed stream in a compressed state, the mixed stream comprising the material and a compressible fluid antisolvent substance, and then causing the mixed stream, including the

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additive, to flow into a downstream region where the compressible fluid antisolvent substance decompresses, and wherein said material and said compressible fluid antisolvent substance are brought together at a location in a conduit having an orifice, said mixed stream flows in the conduit toward said downstream region, and a pressurized gas is introduced into mixed stream in said conduit between said location at which the material and said compressible fluid antisolvent substance are brought together and the orifice.

62 (currently amended). A process ~~according to claim 58, for forming a co-formulation of a material and an additive in which a mixture of a material and an additive is produced by introducing the additive, in a fluid carrier vehicle, into a mixed stream in a compressed state, the mixed stream comprising the material and a compressible fluid antisolvent substance, and then causing the mixed stream, including the additive, to flow into a downstream region where the compressible fluid antisolvent substance decompresses,~~ wherein said mixture flows through a conduit, the flow of the mixture in the conduit is restricted, by a restriction in the conduit between an upstream high pressure zone and a downstream lower pressure zone, and a flow control fluid is introduced into the conduit upstream of the restriction, the pressure of the flow control fluid being equal to or greater than the pressure of the mixture in the conduit upstream of the restriction.

63 (currently amended). A process ~~according to claim 58, for forming a co-formulation of a material and an additive in which a mixture of a material and an additive is produced by introducing the additive, in a fluid carrier vehicle, into a~~

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mixed stream in a compressed state, the mixed stream comprising the material and a compressible fluid antisolvent substance, and then causing the mixed stream, including the additive, to flow into a downstream region where the compressible fluid antisolvent substance decompresses, and wherein said mixture flows along a conduit, and a heat carrier fluid is introduced into the mixture flowing along the conduit.

64 - 65 (cancelled)

66 (currently amended). A process ~~according to claim 63, for~~ forming a co-formulation of a material and an additive in which a mixture of a material and an additive is produced by introducing the additive, in a fluid carrier vehicle, into a mixed stream in a compressed state, the mixed stream comprising the material and a compressible fluid antisolvent substance, and then causing the mixed stream, including the additive, to flow into a downstream region where the compressible fluid antisolvent substance decompresses, wherein the material in the mixed stream is dried in said downstream region, and wherein drying of said material is carried out by entraining particles of said material, in the downstream region, in a stream of gas.

67-71 (cancelled)

72 (currently amended). An apparatus ~~according to claim 69,~~ for the production of particles of a material, comprising:  
means (11, 13, 21, 23, 31, 33) for bringing a stream of a dispersion of the material in a solvent and a stream



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of a compressible fluid antisolvent substance into contact with each other such that the streams combine to form a mixture under conditions such that the antisolvent substance is in a compressible fluid antisolvent state,  
a conduit (17, 27, 37) along which the mixture can flow, the conduit extending downstream from the region where the streams are brought into contact with each other toward an orifice (18, 28, 38),  
means to cause the pressure and temperature of the mixture in the conduit (17, 27, 37) to be such that the substance remains in a compressible fluid antisolvent state along at least part of the conduit (17, 27, 37),  
a downstream region (19, 29, 39) in direct downstream communication with the orifice, and  
means to cause the pressure and temperature conditions in said downstream region to be such that the compressible fluid antisolvent substance in the downstream region is in a gaseous state,  
wherein the means (11, 13, 21, 23, 31, 33) for bringing a stream of a dispersion of the material in a solvent and a stream of a compressible fluid antisolvent substance into contact with each other, and the conduit (17, 27, 37), comprise a "T" or "Y" tube system (15, 25) having limbs for carrying said streams and a stem providing the conduit (17, 27).

73 (currently amended). An apparatus according to claim ~~71~~ 72, wherein the limbs are joined at a junction, and wherein an

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orifice (18, 28, 38) is provided at an end of the stem remote from the junction (15, 25) of the limbs.

74 (cancelled).

75 (currently amended). An apparatus ~~according to claim 73,~~  
for the production of particles of a material, comprising:

means (11, 13, 21, 23, 31, 33) for bringing a stream of a dispersion of the material in a solvent and a stream of a compressible fluid antisolvent substance into contact with each other such that the streams combine to form a mixture under conditions such that the antisolvent substance is in a compressible fluid antisolvent state,

a conduit (17, 27, 37) along which the mixture can flow, the conduit extending downstream from the region where the streams are brought into contact with each other toward an orifice (18, 28, 38),

means to cause the pressure and temperature of the mixture in the conduit (17, 27, 37) to be such that the substance remains in a compressible fluid antisolvent state along at least part of the conduit (17, 27, 37),

a downstream region (19, 29, 39) in direct downstream communication with the orifice,

means to cause the pressure and temperature conditions in said downstream region to be such that the compressible fluid antisolvent substance in the downstream region is in a gaseous state, and introduction means (319, 325) for the introduction of one or more additive and/or modifiers,

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wherein the introduction means comprises an "X" tube arrangement (31, 33, 325, 37), comprising two limbs (31, 33) for introducing the respective streams of dispersion of material and compressible fluid antisolvent substance, a third limb (325) for introducing the additive and/or modifier, and wherein the conduit comprises a fourth limb (37).

76 (currently amended). An apparatus according to claim ~~74~~ 75, wherein the introduction means comprises a further "T" or "Y" tube arrangement (37, 319), located downstream of the point where the dispersion and compressible fluid antisolvent substance are brought into contact with each other.

77 (currently amended). An apparatus ~~according to claim 69,~~  
for the production of particles of a material comprising:

means (11, 13, 21, 23, 31, 33) for bringing a stream of a dispersion of the material in a solvent and a stream of a compressible fluid antisolvent substance into contact with each other such that the streams combine to form a mixture under conditions such that the antisolvent substance is in a compressible fluid antisolvent state,

a conduit (17, 27, 37) along which the mixture can flow, the conduit extending downstream from the region where the streams are brought into contact with each other toward an orifice (18, 28, 38),

means to cause the pressure and temperature of the mixture in the conduit (17, 27, 37) to be such that the substance remains in a compressible fluid

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antisolvent state along at least part of the conduit (17, 27, 37),  
a downstream region (19, 29, 39) in direct downstream communication with the orifice, and  
means to cause the pressure and temperature conditions in said downstream region to be such that the compressible fluid antisolvent substance in the downstream region is in a gaseous state,  
wherein the means to cause the pressure and temperature of the mixture in the conduit (17, 27, 37) to be such that the substance remains in a compressible fluid antisolvent state comprise the conduit (17, 27, 37) having dimensions such as to generate a back pressure in part or all of the conduit between the region where the streams are brought into contact with each other and the orifice (18, 28, 38).

78 (currently amended). An apparatus ~~according to claim 69~~  
for the production of particles of a material comprising:  
means (11, 13, 21, 23, 31, 33) for bringing a stream of a dispersion of the material in a solvent and a stream of a compressible fluid antisolvent substance into contact with each other such that the streams combine to form a mixture under conditions such that the antisolvent substance is in a compressible fluid antisolvent state,  
a conduit (17, 27, 37) along which the mixture can flow, the conduit extending downstream from the region where the streams are brought into contact with each other toward an orifice (18, 28, 38),

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means to cause the pressure and temperature of the mixture in the conduit (17, 27, 37) to be such that the substance remains in a compressible fluid antisolvent state along at least part of the conduit (17, 27, 37),

a downstream region (19, 29, 39) in direct downstream communication with the orifice, and

means to cause the pressure and temperature conditions in said downstream region to be such that the compressible fluid antisolvent substance in the downstream region is in a gaseous state,

said apparatus also comprising pressurized gas introduction means (214) to introduce a pressurized gas directly into the conduit (27) is provided.

79 (cancelled).

80 (currently amended). An apparatus ~~according to claim 78,~~  
for the production of particles of a material comprising:

means (11, 13, 21, 23, 31, 33) for bringing a stream of a dispersion of the material in a solvent and a stream of a compressible fluid antisolvent substance into contact with each other such that the streams combine to form a mixture under conditions such that the antisolvent substance is in a compressible fluid antisolvent state,

a conduit (17, 27, 37) along which the mixture can flow, the conduit extending downstream from the region where the streams are brought into contact with each other toward an orifice (18, 28, 38),

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means to cause the pressure and temperature of the mixture in the conduit (17, 27, 37) to be such that the substance remains in a compressible fluid antisolvent state along at least part of the conduit (17, 27, 37),

a downstream region (19, 29, 39) in direct downstream communication with the orifice,

means to cause the pressure and temperature conditions in said downstream region to be such that the compressible fluid antisolvent substance in the downstream region is in a gaseous state, and

drying means to dry particles of said material which are formed as a result of the mixture of said streams,

wherein the drying means introduces a stream of heated air around the orifice.

81 (cancelled).